

What is claimed is:

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*B1* 1. A method to desensitize a receptor selected from the group consisting of a B cell antigen receptor, a pro-B cell receptor, a pre-B cell receptor and an Ig Fc receptor, said method comprising: contacting a receptor selected from the group consisting of a B cell antigen receptor, a pro-B cell receptor, a pre-B cell receptor, an Ig Fc receptor, and a natural killer (NK) cell receptor, with a regulatory compound, wherein said receptor has a transducer component and an extracellular ligand binding component;

wherein contact with said regulatory compound: (1) causes a dissociation of said extracellular ligand binding component from said transducer component when said components are associated with each other prior to contact with said compound; or (2) inhibits association of said extracellular ligand binding component with said transducer component when said components are dissociated from each other prior to contact with said compound.

~~2. The method of Claim 1, wherein said regulatory compound binds to said transducer component.~~

~~3. The method of Claim 1, wherein said regulatory compound binds to said extracellular ligand binding component.~~

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*B2* 4. The method of Claim 1, wherein said regulatory compound inhibits association of said extracellular ligand binding component with said transducer component when said components are dissociated from each other.

5. The method of Claim 4, wherein said regulatory compound selectively binds to a portion of said transducer component that contacts a portion of said extracellular ligand binding component when said receptor is bound by its natural ligand, thereby inhibiting contact of said transducer component with said extracellular ligand binding component.

6. The method of Claim 4, wherein said regulatory compound selectively binds to a portion of said transducer component which contacts a portion of said extracellular ligand binding component that is phosphorylated when said receptor is bound by its natural ligand, thereby inhibiting phosphorylation of said extracellular ligand binding component.

~~7. The method of Claim 1, wherein said regulatory compound is selected from the group consisting of an antibody, a peptide and a mimotope thereof.~~

~~8. The method of Claim 1, wherein said regulatory compound is an antibody.~~

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9. The method of Claim 8, wherein said antibody is monovalent.

10. The method of Claim 8, wherein said antibody is divalent.

~~11. The method of Claim 8, wherein said antibody binds to said transducer component.~~

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12. The method of Claim 8, wherein said antibody is a bi-specific antibody comprising:

a. a first portion which binds to said receptor and: (1) causes a dissociation of said extracellular ligand binding component from said transducer component when said components are associated with each other prior to contact with said compound; or (2) inhibits association of said extracellular ligand binding component with said transducer component when said components are dissociated from each other prior to contact with said compound; and

b. a second portion which selectively binds to a cell surface molecule expressed by a cell which expresses said receptor.

~~8 13.~~ The method of Claim ~~12~~<sup>7</sup>, wherein said second portion binds to a cell surface molecule which is expressed by an autoreactive B cell.

~~9 14.~~ The method of Claim ~~12~~<sup>7</sup>, wherein said second portion binds to an antigen binding region of said B cell antigen receptor.

~~15. The method of Claim 1, wherein said receptor is selected from the group consisting of a B cell antigen receptor, a pro-B cell receptor, and a pre-B cell receptor.~~

16. The method of Claim 15, wherein said transducer component is selected from the group consisting of Ig $\alpha$  and Ig $\beta$ .

17. The method of Claim 15, wherein said regulatory compound selectively binds to said transducer component and inhibits association of said extracellular ligand binding component with said transducer component.

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18. The method of Claim 15, wherein said extracellular binding component comprises an mIg selected from the group consisting of IgD and IgM.

19. The method of Claim 15, wherein said B cell antigen receptor selectively binds to an antigen associated with an autoimmune disease.

20. The method of Claim 15, wherein said B cell antigen receptor selectively binds to an antigen associated with a graft cell.

21. The method of Claim 15, wherein said receptor is expressed by a cell selected from the group consisting of an autoreactive B cell, a B cell comprising a B cell antigen receptor that selectively binds to an antigen on a graft, a B cell lymphoma and a chronic lymphocytic leukemia cell.

22. The method of Claim 15, wherein said regulatory compound is administered to a patient that has an autoimmune disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, insulin dependent diabetes mellitus, multiple sclerosis, myasthenia gravis, Grave's disease, autoimmune hemolytic anemia, autoimmune thrombocytopenia purpura, Goodpasture's syndrome, pemphigus vulgaris, acute rheumatic fever, post-streptococcal glomerulonephritis, and polyarteritis nodosa.

~~23. The method of Claim 1, wherein said receptor is a human Ig Fc receptor selected from the group consisting of Fc $\alpha$ RI, Fc $\epsilon$ RI, Fc $\gamma$ RI, Fc $\gamma$ RIIa, Fc $\gamma$ RIIb, Fc $\gamma$ RIIc, Fc $\gamma$ RIIb, and wherein said regulatory compound selectively binds to an extracellular ligand binding domain of said Fc receptor.~~

24. The method of Claim 23, wherein said extracellular binding component comprises an  $\alpha$  receptor.

25. The method of Claim 23, wherein said receptor is an Fc $\epsilon$ RI receptor comprising an  $\alpha$  receptor extracellular ligand binding component and a  $\beta/\gamma$  transducer component.

26. The method of Claim 23, wherein said receptor is expressed by a cell selected from the group consisting of a mast cell and a basophil.

27. The method of Claim 23, wherein said regulatory compound is administered to a patient that has a condition associated with inflammation.

28. The method of Claim 27, wherein said condition is associated with allergic inflammation.

29. The method of Claim 1, wherein said receptor is an NK receptor comprising an extracellular ligand binding component KIRDL and a transducer component DAP12.

Sub B6 30. The method of Claim 1, wherein said regulatory compound is administered to a patient by way of a therapeutic composition comprising a pharmaceutically acceptable carrier and said compound.

16 31. The method of Claim <sup>15</sup>~~30~~, wherein said therapeutic composition is administered *in vivo*.

17 32. The method of Claim <sup>15</sup>~~30~~, wherein said therapeutic composition is administered *ex vivo*.

Sub B7 33. The method of Claim 1, wherein said regulatory compound is contacted with said receptor in an *in vitro* assay.

34. An isolated regulatory compound that desensitizes a receptor selected from the group consisting of a B cell antigen receptor, an Ig Fc receptor, and an NK receptor, wherein said receptor has an extracellular ligand binding component and a transducer component, said regulatory compound being identified by its ability to selectively bind to said receptor and upon said binding: (1) induces said extracellular ligand binding component to dissociate from said transducer component; and/or (2) inhibits said extracellular ligand binding component from associating with said transducer component.

35. The isolated regulatory compound of Claim 34, wherein said isolated regulatory compound is selected from the group consisting of a peptide, an antibody and a mimetope thereof.

36. The isolated regulatory compound of Claim 34, wherein said compound is an antibody.

37. The isolated regulatory compound of Claim 36, wherein said antibody is monovalent.

38. The isolated regulatory compound of Claim 36, wherein said antibody is a bi-specific antibody comprising:

a. a first portion which binds to said receptor and: (1) causes a dissociation of said extracellular ligand binding component from said transducer component when said components are associated with each other prior to contact with said compound; or (2) inhibits association of said extracellular ligand binding component with said transducer component when said components are dissociated from each other prior to contact with said compound; and

b. a second portion which selectively binds to a cell surface molecule expressed by a cell which expresses said receptor.

39. The isolated regulatory compound of Claim 36, wherein said antibody binds to said transducer component.

40. The isolated regulatory compound of Claim 36, wherein said antibody inhibits said extracellular ligand binding component from associating with said transducer component.

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44. A method to identify compounds useful for desensitizing a receptor, comprising:

a. contacting with a putative regulatory compound a receptor selected from the group consisting of a B cell antigen receptor, a pro-B cell receptor, a pre-B cell receptor, an Fc receptor, and an NK receptor, wherein said receptor comprises an extracellular ligand binding component and at least one transducer component, and wherein said extracellular ligand binding component is associated with said transducer component prior to contact of said receptor with said putative regulatory compound; and,

b. detecting whether said putative regulatory compound, when contacted with said receptor, causes said extracellular ligand binding component to dissociate from said transducer component, wherein a putative regulatory compound that causes said dissociation is identified as a regulatory compound.

45. The method of Claim 44, wherein said receptor is expressed by a cell.

46. The method of Claim 44, wherein said step of detecting comprises a bioassay that measures the ability of said receptor to transduce a signal as a result of stimulation of said receptor, and wherein a reduced ability of said receptor to transduce a signal as a result of stimulation when contacted with said putative regulatory compound, as compared to in the absence of contact with said compound, indicates that said compound desensitizes said receptor.

47. A method to identify compounds useful for desensitizing a receptor, comprising:

a. contacting with a putative regulatory compound a receptor selected from the group consisting of a B cell antigen receptor, an Fc receptor, and an NK receptor, wherein said receptor includes an extracellular ligand binding component and at least one transducer component, and wherein said extracellular ligand binding component is not associated with said transducer component prior to contact with said putative regulatory compound;

b. detecting whether said putative regulatory compound, when contacted with said receptor, inhibits said extracellular ligand binding component from associating with said transducer component, wherein a putative regulatory compound that inhibits said association is identified as a regulatory compound.

48. The method of Claim 47, wherein said extracellular ligand binding component is not associated with said transducer component as a result of binding of said receptor by a stimulator.



49. A method for sensitizing or enhancing or prolonging sensitization of a receptor selected from the group consisting of BCR, pro-BCR, pre-BCR, FcR, and an NK receptor, comprising contacting a compound with a receptor that has an extracellular ligand binding component and a transducer component, wherein said compound: (1) causes said extracellular ligand binding component to associate with said transducer component when said two components are not associated with each other prior to contact by said compound; or (2) prolongs or enhances the time over which said extracellular ligand binding component is associated with said transducer component when said components are associated prior to contact by said compound, thereby sensitizing said receptor.